



# Towards a quantitative perspective in Networks of Bio-inspired Processors (NBP)

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# Outline

# Introduction

- Complex and hard problems in computation
  - NP complete
- Methods and paradigms to solve these problems in an efficient way
  - Bio-inspired models based on formal languages
  - Discrete approximations

# Bio-inspired computational models

- Inspired from the nature: How nature computes?
  - Efficiently
  - Distributed
  - Massively parallelism
  - In a real time
- First step:
  - Mathematical and computer science goals
  - After biological goals.

# NBP model

- Networks of bio-inspired processors
  - Maturity
  - Solves NP complete problems
    - Polynomial time with lineal number of resources
  - Efficiency
  - Extensibility
  - Simplicity

# Estado del arte: NBP

Características y poder computacional :

- Universales y computacionalmente completas
  - Resuelven problemas NP-completos
- Eficientes
  - Complejidad espacial: Número lineal de recursos
  - Complejidad temporal: polinomial
- Simples y Expresivas
- Extensibles / Escalables
- Distribuidas y paralelas

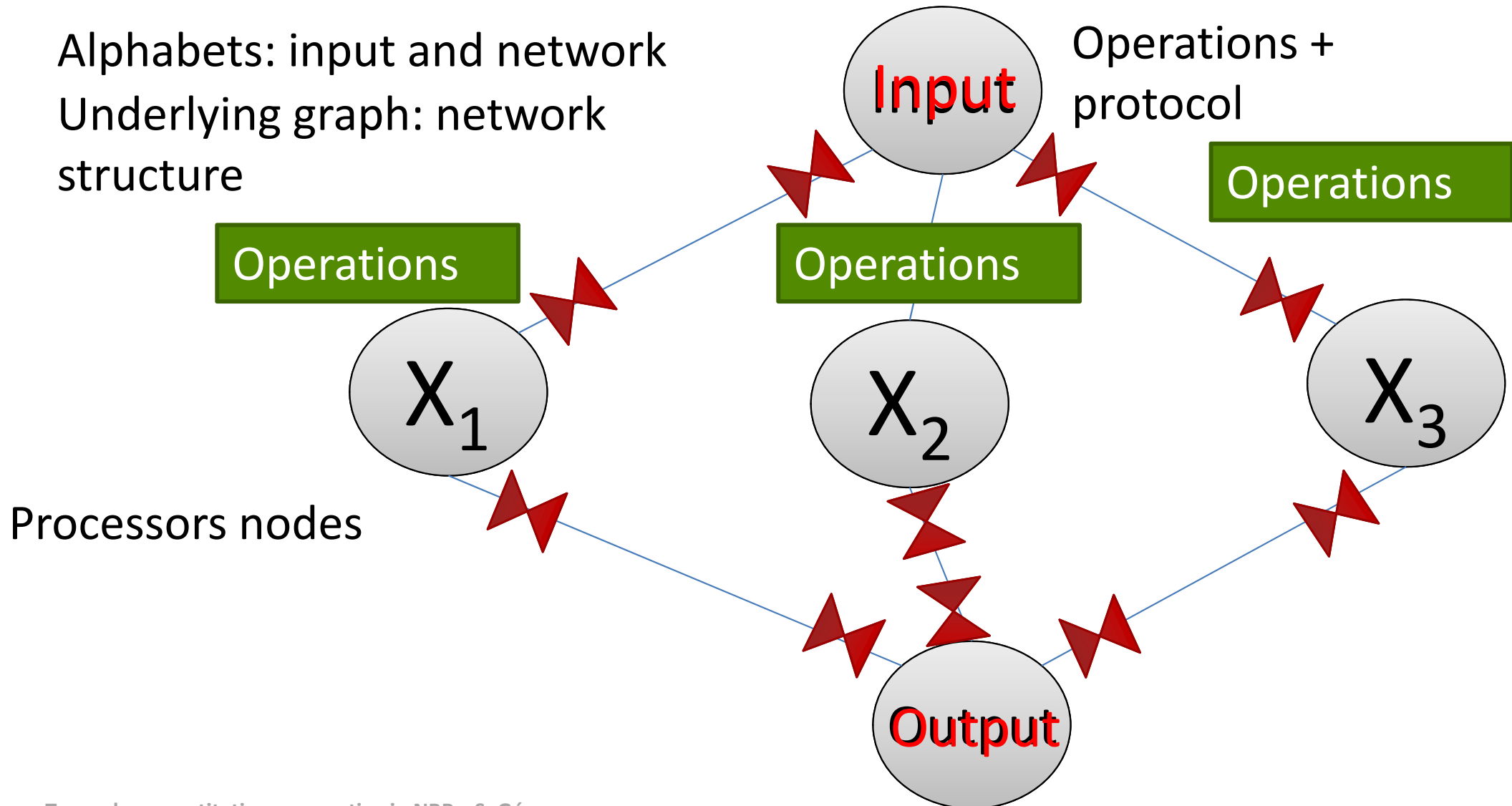
# NBP model

Networks of bio-inspired processors – NBP [Mitrana,2001].

- Processors as generating languages devices
- Located in nodes of a network
- Data processing (as ADN strings) based on rewriting rules of a grammar
- Protocol Communication in the connections between nodes
- Parallelism in the processing and the communication phases

# NBP model

Alphabets: input and network  
Underlying graph: network structure

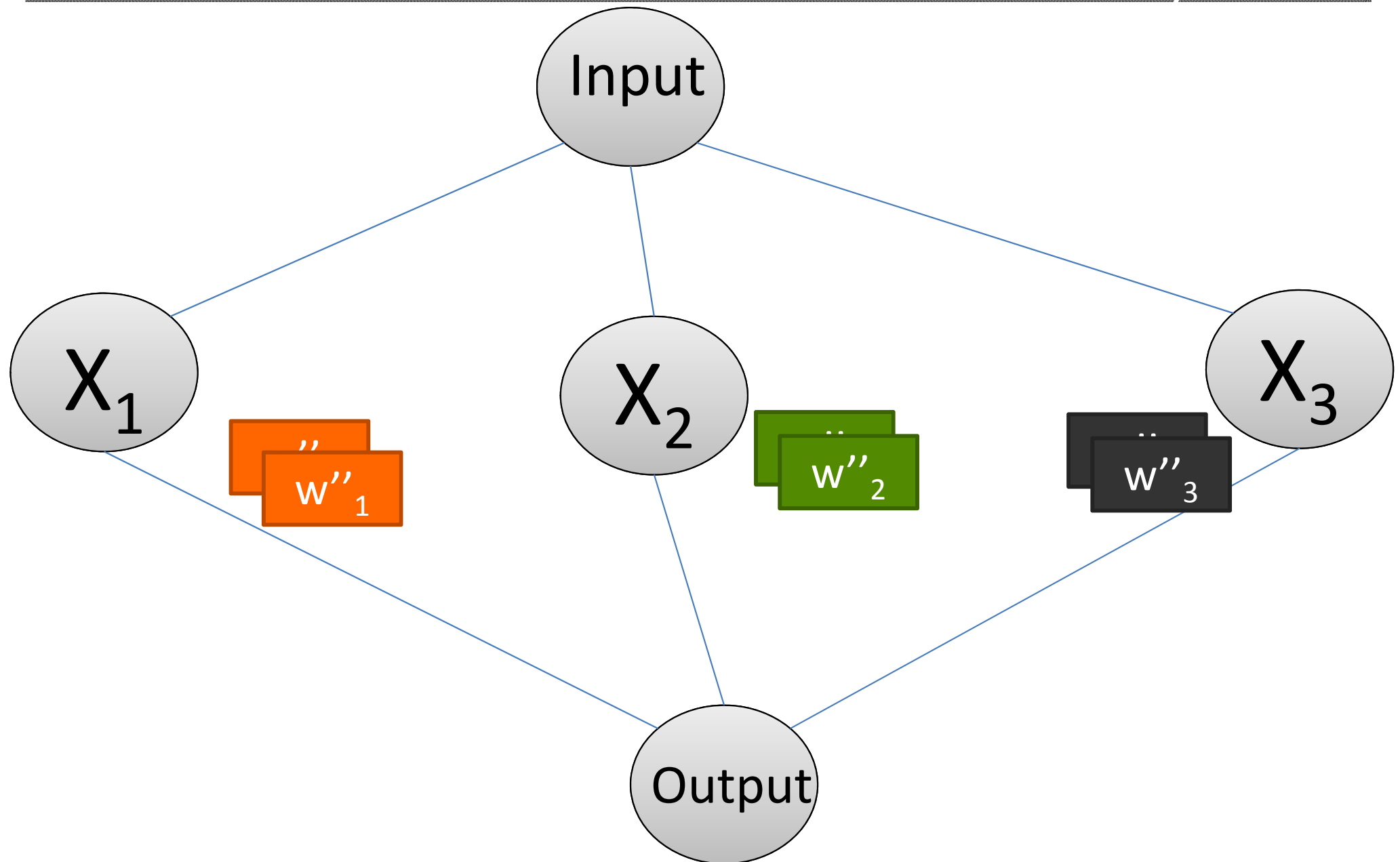




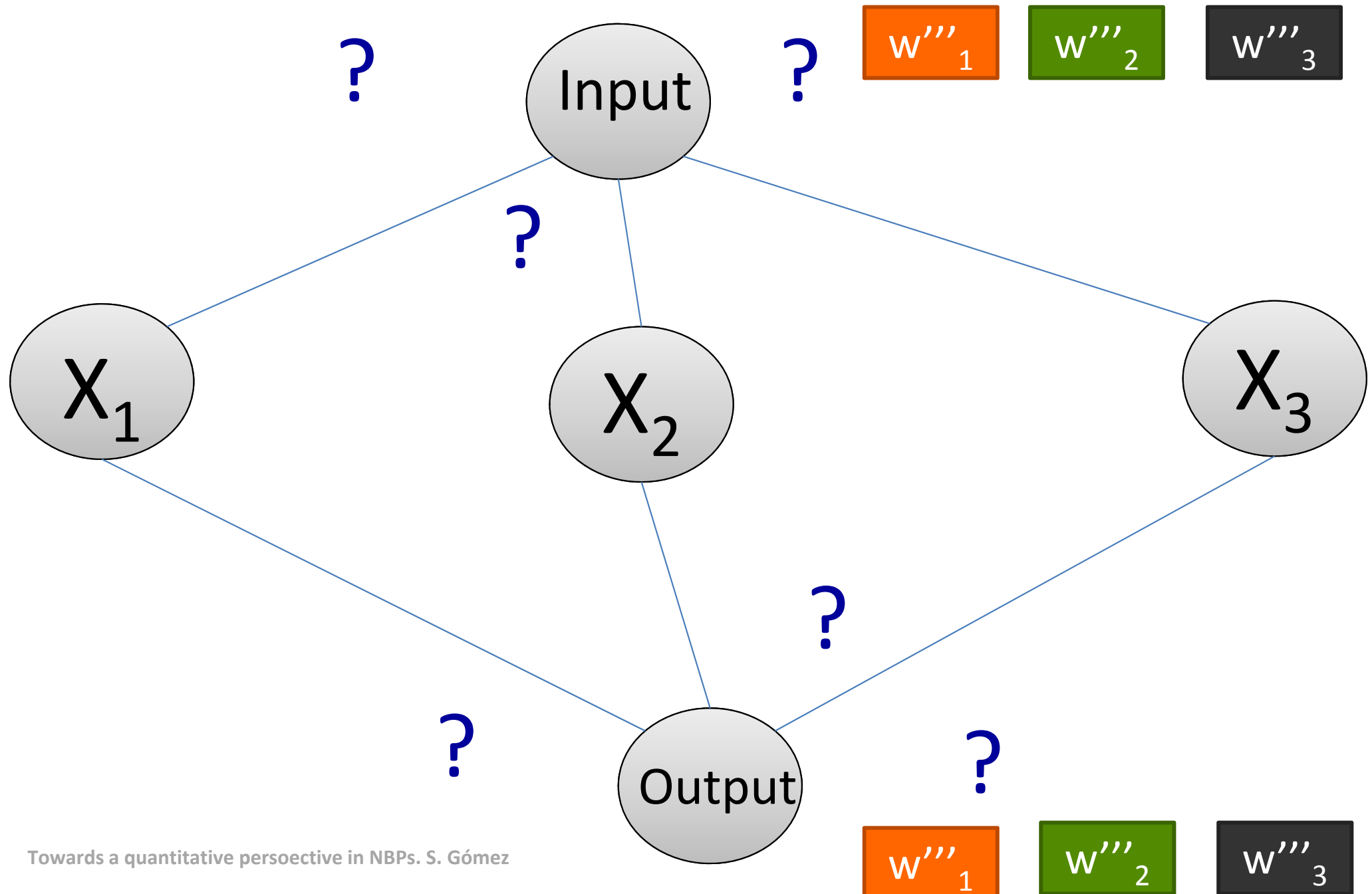
# Objetivos, justificación y motivación

- Acercamiento a la realidad biológica
- Orientación a un carácter cuantitativo
- Cambio en el enfoque del dominio de los problemas

## NBP Metamodel Dynamic



## NBP Metamodel Dynamic



# NBP Metamodel Dynamic

## Formal definitions

**$\Gamma$  configuration** :  $C: X_G \rightarrow 2^{V^*}$

**Initial  $\Gamma$  configuration** in  $w \in V^*$

$$C_0^{(w)}(X_I) = \{w\} \text{ y } C_0^{(w)}(x) = \emptyset \quad \forall x \in X_G - \{X_I\}$$

Evolution step

$$C \Rightarrow C' \text{ sii}$$

$$C'(x) = M_x^{\alpha(x)}(C(x)) \quad \forall x \in X_G$$

Communication step

$$C \vdash C' \text{ sii}$$

$$C'(x) = \left( C(x) - \tau_x(C(x)) \right) \cup \bigcup_{\{x,y\} \in E_G} (\tau_y(C(y)) \cap \rho_x(C(y)))$$

# NBP Metamodel Dynamic

## Formal definitions

**$\Gamma$  Computation** in  $w \in V^* : C_0^{(w)}, C_1^{(w)}, C_2^{(w)} \dots,$   

$$C_{2i}^{(w)} \Rightarrow C_{2i+1}^{(w)} \quad \forall C_{2i+1}^{(w)} \vdash C_{2i+2}^{(w)} \quad \forall i \geq 0$$

A **computation** halts :

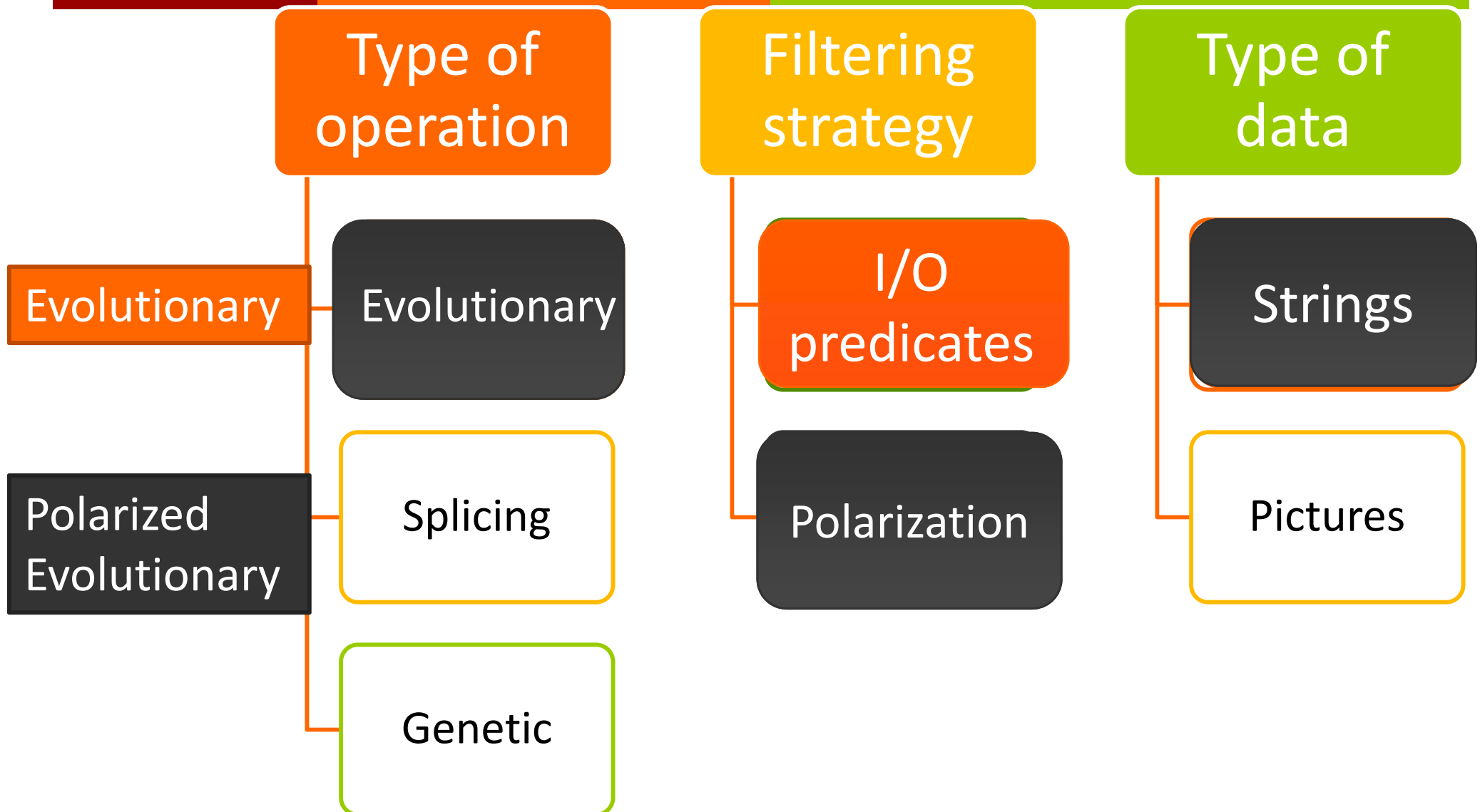
- i.  $X_0$  is non-empty : *acceptation computation*.
- ii. There are two identical configurations obtained in consecutive steps

**Accepted language** by  $\Gamma$  is

$L(\Gamma) =$

$\{ w \in V^* \mid \Gamma \text{ computation in } w \text{ accepting computation} \}$

# NBP model classification



# Networks of Evolutionary Processors: NEP



# Networks of Evolutionary Processors:

## NEP

➤ **Evolutionary rule:** point mutations in a DNA sequence (insertion, deletion or substitution of a pair of nucleotides).

➤  $\sigma: a \rightarrow b$  such that  $a, b \in V \cup \varepsilon$

➤ Action rule:  $\alpha = \{*, l, r\}$

Evolutionary rule $\sigma$	Definition	Action rule $\sigma$
Substitution	$a, b \neq \varepsilon$	$\alpha = \{*\}$
Deletion	$a \neq \varepsilon \vee b = \varepsilon$	$\alpha = \{*, l, r\}$
Insertion	$a = \varepsilon \vee b \neq \varepsilon$	

➤  $Sub_V, Del_V \in Ins_V$  set of all rules over  $V$



# Networks of Evolutionary Processors: NEP

- Filtering strategy:  $\beta \in \{s, w\}$ 
  - $s$  : *strong*
  - $w$  : *weak*
- Set of permitting/forbidding symbols

Symbols	Input	Output	Strong	Weak
Permitting	PI	PO	All	1 or more
Forbidding	FI	FO	None	None

# Networks of Evolutionary Processors: NEP

**Definition:** Evolutionary processor associated to the node  $x$  is a 5-tuple  $(M_x, PI_x, FI_x, PO_x, FO_x)$  where:

- $M_x$  is a finite set of evolutionary rules such that tal que  $M_x \subseteq Sub_V$ ,  $M_x \subseteq Del_V$  or  $M_x \subseteq Ins_V$
- $PI_x, FI_x$  are the permitting/forbidding contexts/symbols respectively, such that  $PI_x \cap FI_x = \emptyset$
- $PO_x, FO_x$  are the permitting/forbidding contexts/symbols respectively, such that  $PO_x \cap FO_x = \emptyset$

# Networks of Evolutionary Processors:

## NEP

**Networks of Evolutionary Processors** – NEP is a 8-tuple  $(V, U, G, N, \alpha, \beta, X_I, X_O)$

- $V, U$  tal que  $V \subseteq U$
- $G = (X_G, E_G)$  **underlying graph.**
- $N: X_G \rightarrow EP_U$  mapping  $x \in X_G$   
with  $N(x) = (M_x, Pl_x, Fl_x, PO_x, FO_x)$
- $\alpha: X_G \rightarrow \{*, l, r\}; \alpha(x)$
- $\beta: X_G \rightarrow \{s, w\}$  I/O filters
- $X_I, X_O$  are input and output nodes

# Polarized NEP



# Polarized NEP

- Networks of Polarized Evolutionary Processors – NPEP [Mittrana,2012].
- **Polarization**: filter strategy. Sign={-,0,+}
- **Valuation mapping** for strings.
- **Filtering protocol**: sign of the word **but does not** real numeric value.
- Simulates cellular communication by ion channels

# Polarized NEP

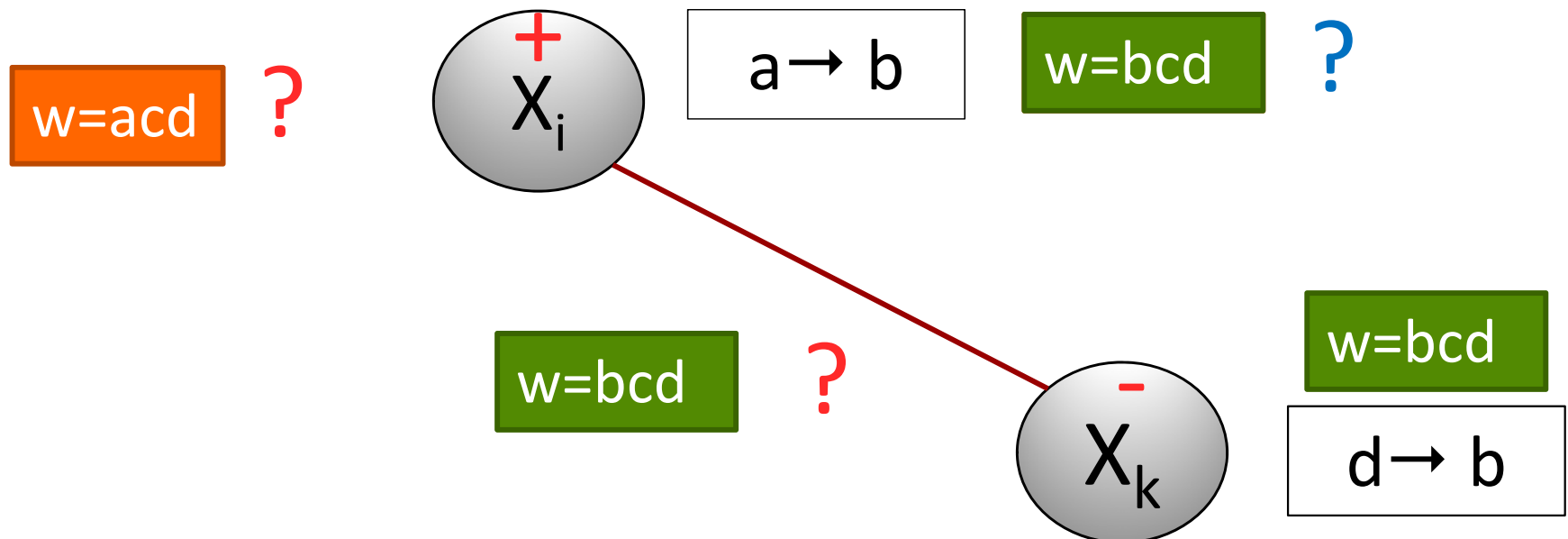
➤ Valuation function:  $\varphi$  de  $U^*$  en  $\mathbb{Z}$

$U=\{a,b,c\}$

$\varphi(a)=1$

$\varphi(b)=-1$

➤ Polarity (sign) to each node



# Polarized NEP

**Polarized Evolutionary Processor** over  $V$  is a pair  $(M, \alpha)$ :

➤  $M \subseteq Sub_V, M \subseteq Del_V$  or  $M \subseteq Ins_V$

➤  $\alpha \in \{-, 0, +\}$  is the node polarity

**NPEP is a 7-tuple  $\Gamma = (V, U, G, N, \varphi, X_I, X_O)$**  where

➤  $V, U, V \subseteq U$

➤  $G = (X_G, E_G)$  underlying graph

➤  $N: X_G \rightarrow EP_U$  is a mapping from  $x \in X_G$  to  $N(x) = (M_x, \alpha_x)$

➤  $\varphi$  is a valuation from  $U^*$  to  $\mathbb{Z}$

➤  $X_I, X_O$  are the input and output nodes respectively

# Polarized NEP Dynamics

**$\Gamma$  Configuration** = NEP model

**$\Gamma$  Initial configuration** = NEP model

Evolutionary step

$$C \Rightarrow C' \text{ s.t.}$$

$$C'(x) = M_x(C(x)) \quad \forall x \in X_G$$

Communication step

$$C \vdash C' \text{ s.t.}$$

$$C(x) = (C(x) \setminus \{w \in C(x) \mid \varphi(w) \neq \alpha_x\})$$

$$\cup \bigcup_{\{x,y\} \in E_G} (w \in C(y) \mid \alpha_y \neq \varphi(w) = \alpha_x) \quad \forall x \in X_G$$



# Qualitative or Quantitative aspects?

- NPEP is motivated by mathematical and computer science goals, but not necessarily by biological goals.
- Application of NEP in other different domains
- It is necessary to consider not only their qualitative perspective but also the quantitative one.
- Quantitative aspects are a “sine qua non” condition within biological reality
- Although it's true that NPEP incorporates a numerical evaluation over the data that processes, this is not used from quantitative perspective.

# Quantitative NEPs



# Quantitative NEPs

In cellular and biological phenomena:

- Compare software simulation vs experiments
- Quantitative valuations
  - Concentrations, gradients, thresholds, etc...
- It is necessary a NEP model with quantitative elements: **QNEPs**

# Parametric NEP: PNPEP

- First model of the **Quantitative NEP** family.
- Polarized NEP extension
- Polarized NEP has a valuation mapping:
  - But it is only qualitative valuation.
- Now, we want to compute the **exact weighth** of valuation of a word

# Parametric NEP: PNPEP

➤ In NPEP:  $\varphi$  is a valuation from  $U^*$  to  $\mathbb{Z}$

➤ If  $U=\{n,N,k,K,p\}$

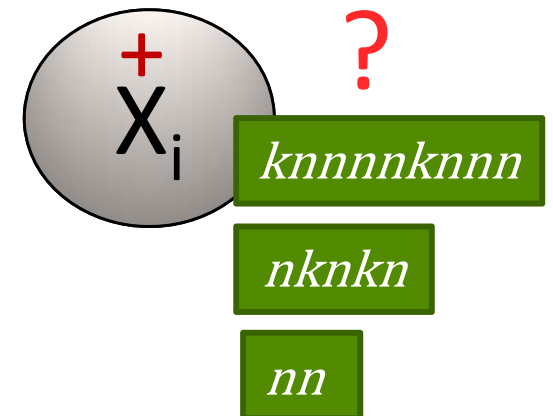
$\varphi(n) = 1$	$\varphi(k) = -1$
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Word	Mapping valuation	Polarity
<i>nknkn</i>	+	+
<i>knnnnknnn</i>	+	+
<i>nn</i>	+	+

*knnnnknnn*

*nknkn*

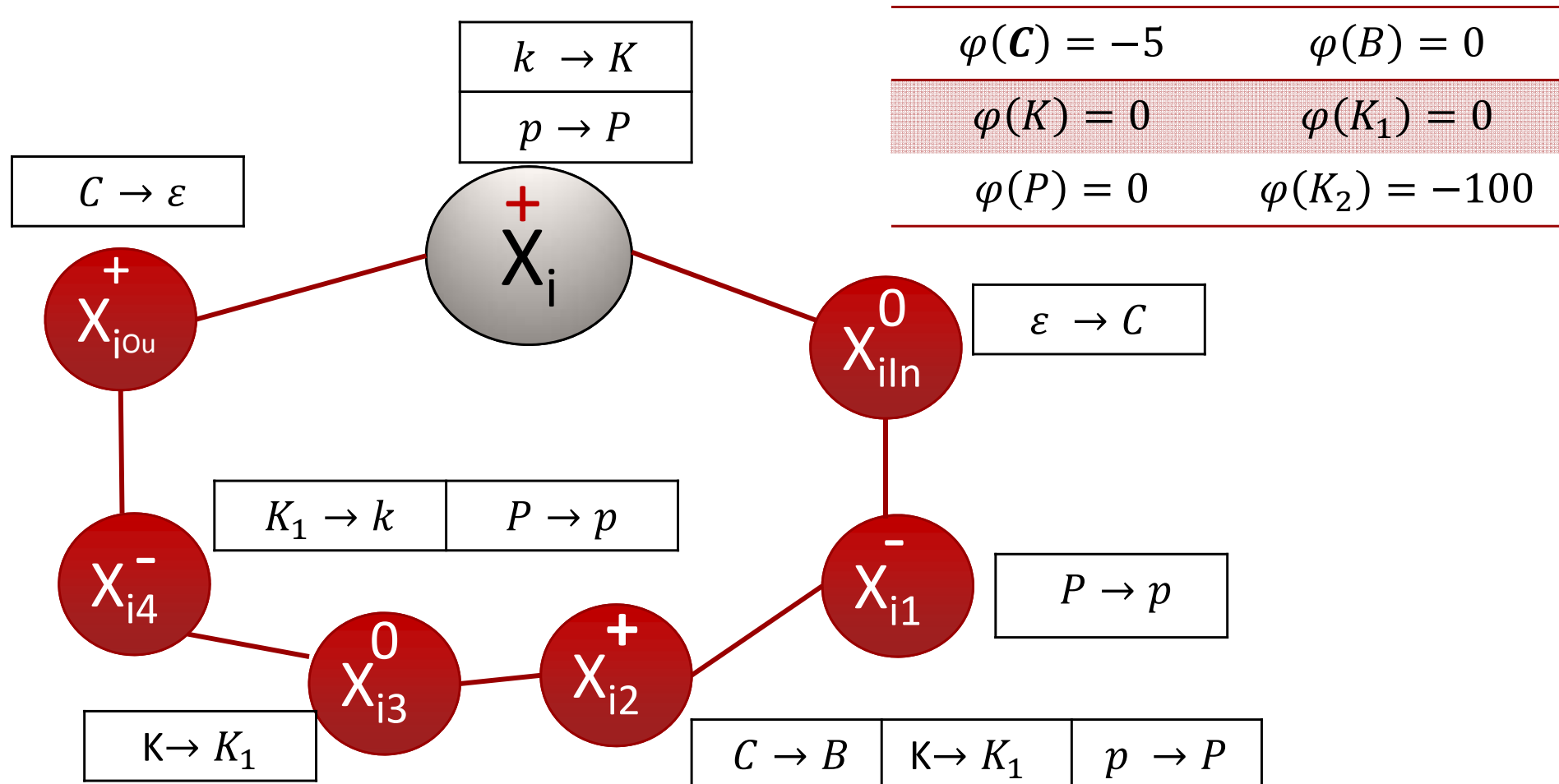
*nn*



Word	Mapping valuation	Result
<i>nknkn</i>	+	1
<i>knnnnknnn</i>	+	5
<i>nn</i>	+	2

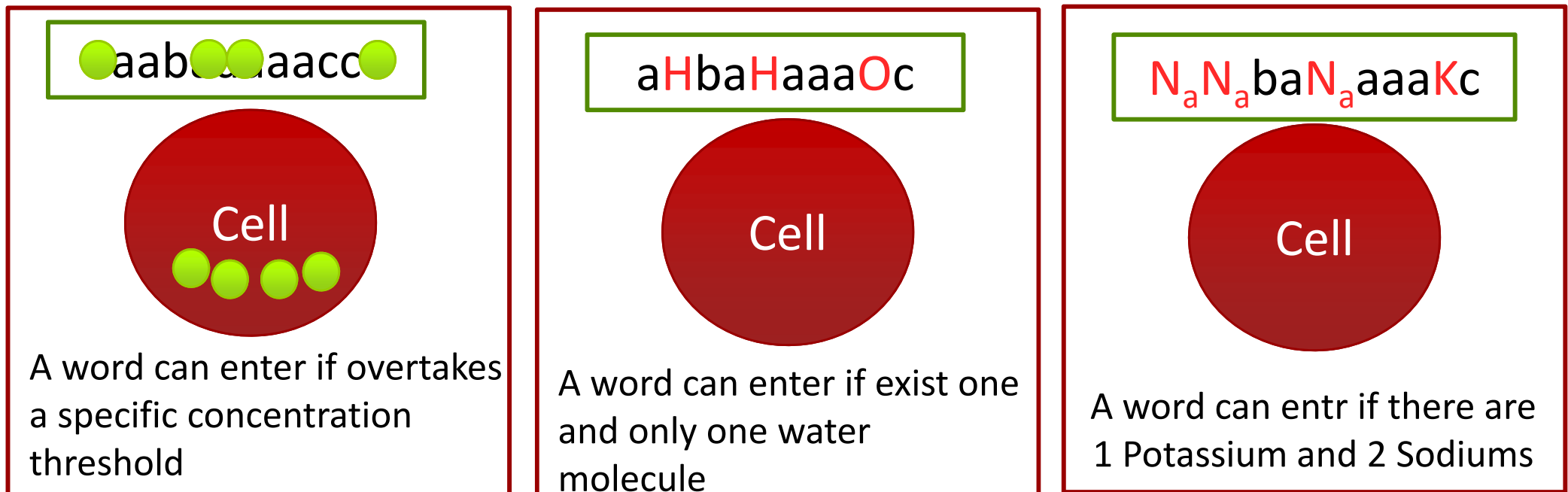
# NPEP Valuation....

- Must be filtering words having a concentration  $> 5$  of symbols  $p$
- To aggregate symbols  $D, P, C, K, P$  in  $U$  alphabet



# Parametric NEP: PNPEP

➔ To fill this lack..

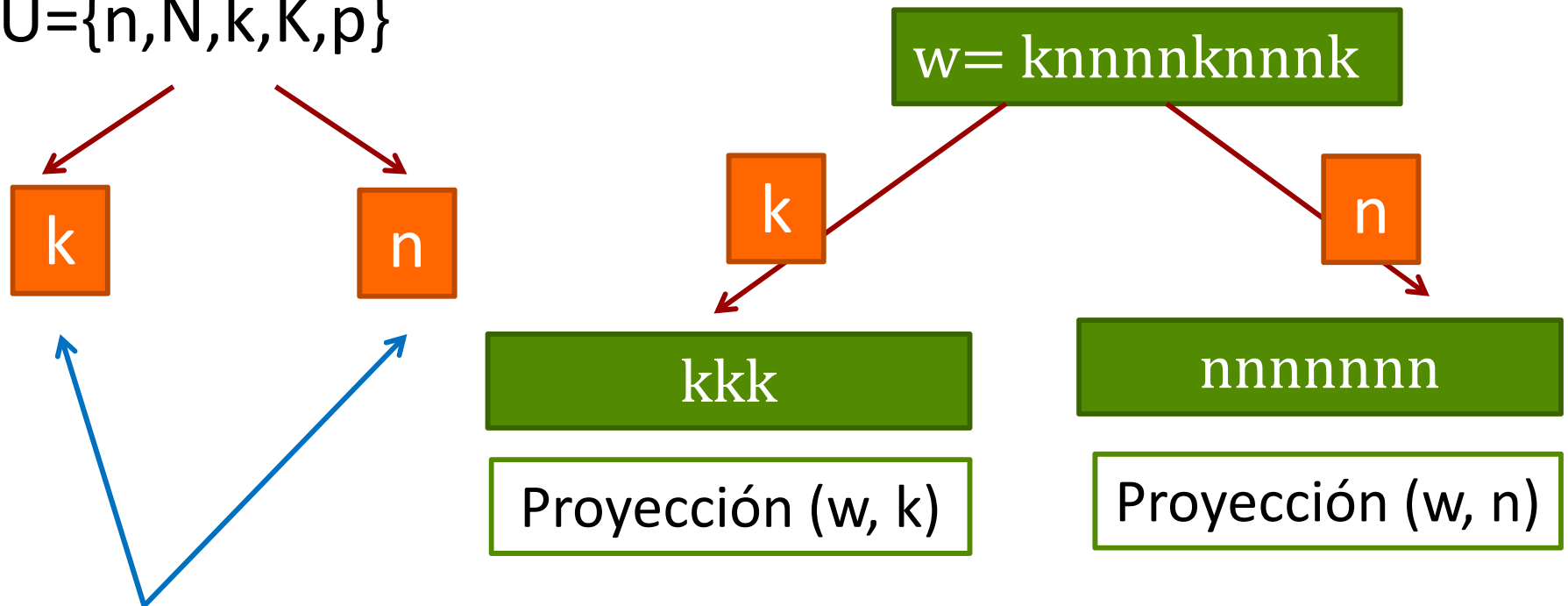


# Parametric NEP: PNPEP

New elements:

➤ Projection function over words

Si  $U = \{n, N, k, K, p\}$

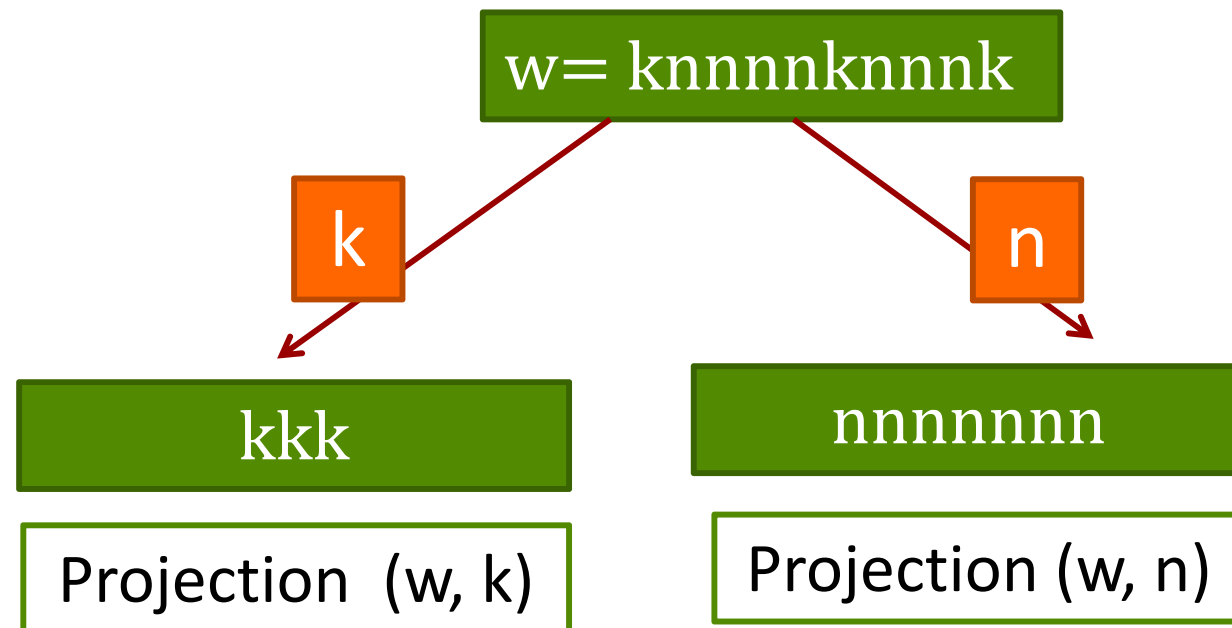


It is necessary a set of partitions over  $U$



# Parametric NEP: PNPEP

➤ Evaluation of the projection over a specific interval



$5 \leq \text{Potassium concentration} \leq 10$      $100 \leq \text{Soddiun comcentration} \leq 200$

Polarity is divided between less generic intervals

# Parametric NEP: PNPEP

➤ Valuation mapping NPEP is  $\varphi: U^* \rightarrow \mathbb{Z}$

➤ **Redefining**  $\varphi: U^* \rightarrow \mathbb{Z}^m$

➤ If  $2^U = P = \{P_1, P_2, \dots, P_m\}$  then

*Projection function:*

$$\pi_j(w, P_j) = a'_1, a'_2, \dots, a'_k \quad \text{where } a'_i = \begin{cases} a_i & \text{if } a_i \in P_j \\ \varepsilon & \text{otherwise} \end{cases}$$

➤ If  $\Pi = \{\pi_1, \pi_2, \dots, \pi_m\}$  then

$$\varphi(w) = \varphi_i(\pi_i(w, P_i)) \text{ for all } i \in \{1, 2, \dots, m\}$$

# Parametric NEP: PNPEP

- Polarized NEP: polarity denoted by  $\alpha \in \{-, 0, +\}$
- New polarization: **labels for  $\alpha$** 
  - Changing the notation:  $\alpha \in \{(-\infty, 0), \{0\}, (0, +\infty)\}$
- Valuating the concentration of  $p \geq 5$  then
  - $\alpha \in \{(-\infty, 0), \{0\}, (0, 5), [5, +\infty]\}$

Classic notation	Parametric Polarized NEP
$\alpha \in \{(-\infty, 0), \{0\}, (0, +\infty)\} =$ $\alpha \in \{l_0, l_1, l_2\}$	$\alpha \in \{l_0, l_1, l_2 \dots l_m\}$ $\bigcup_{i=0}^m l_i = \mathbb{Z}$

# Parametric NEP: PNPEP

➤  $\alpha \in \{(-\infty, 0), \{0\}, (0, 5), [5, +\infty)\}$

$w_1 = \text{knnnnknknk}$

↓  
7

Projection ( $w_1, k$ ):

kkkkkkk

$w_2 = \text{nknkn}$

↓  
2

Projection ( $w_2, k$ ):

kk

$w_3 = \text{nn}$

↓  
0

$\varepsilon$

Projection ( $w_3, k$ ):

$\alpha \in \{(-\infty, 0), \{0\}, (0, 5), [5, +\infty)\} = \{l_0, l_1, l_2, l_3\}$

$l_0$

$l_1$

$l_2$

$l_3$

# Parametric NEP: PNPEP

A **parametric polarized evolutionary processor** is a 3-tuple  $(M, S, \alpha)$ :

- $M \subseteq Sub_V, M \subseteq Del_V$  or  $M \subseteq Ins_V$
- $S \subseteq P$  is the set of partitions of  $U$  that this processor evaluates
- $\alpha \in \{l_x^0, l_x^1, l_x^2, \dots, l_x^m\}$ ,  $m = \text{card}(S)$

Is the polarity partition

# Parametric NEP: PNPEP

## Networks of Parametric Polarized Evolutionary Processors –

PNPEP is a 8-tuple  $\Gamma = (V, U, P, G, R, \varphi, X_I, X_O)$

➤  $V, U$  such that  $V \subseteq U$

➤  $P$  is a partition over  $U$

➤  $G = (X_G, E_G)$  is a underlying graph

➤  $N: X_G \rightarrow EP_U$  is the mapping from node to processors  
 $N(x) = (M_x, S_x, \alpha_x)$

➤  $\varphi$  is a valuation from  $U^*$  to  $\mathbb{Z}^m$

➤  $X_I, X_O$  are the input and output node respectively

# Parametric NEP: PNPEP

$\mathbf{V} = \{s, S, p, P, v, V, A\}$  y  $\mathbf{U} = \{n, N, k, K, b, B, a, t, q, f, \tilde{n}\}$

$P = \{P_0 = \{n\}, P_1 = \{k\}, P_2 = \{K, N, K, g, B, a, q, f, \tilde{n}, t\}\}$

$\varphi(p) = 1$	$\varphi(k) = -1$
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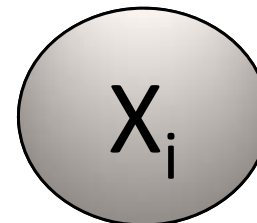
$\alpha$ Intervalo polarización	$\alpha_{x_i}$	S
$[0, 5), [5, +\infty)$	$l_{xi}^{-1}$	$P_1$

$w_1 = knnnnknknk$

kkkkkkkk

$w_2 = nknkn$

$w_3 = nn$



# Parametric NEP: Dynamic

**$\Gamma$  Configuration** =  $C: X_G \rightarrow 2^{U^*}$

**$\Gamma$  Initial configuration** = NPEP model

Evolutionary step

$$C \Rightarrow C' \text{ s.t.}$$

$$C'(x) = M_x(C(x)) \forall x \in X_G$$

Communication step

$$C \vdash C' \text{ s.t.}$$

$$C'(x) = (C(x) \setminus \{w \in C(x) \mid \varphi_i(w) = \varphi(\pi_i(w)) \notin \alpha_{x,i} \forall \pi_i \in \Pi\}) \cup \bigcup_{x,y \in E_G} (\{w \in C(y) \mid \varphi_i(w) = \varphi(\pi_i(w)) \in \alpha_{x,i} \exists \pi_i \in \Pi\})$$



# Na – K Pump simulation using Parametric NEP



# Conceptos básicos

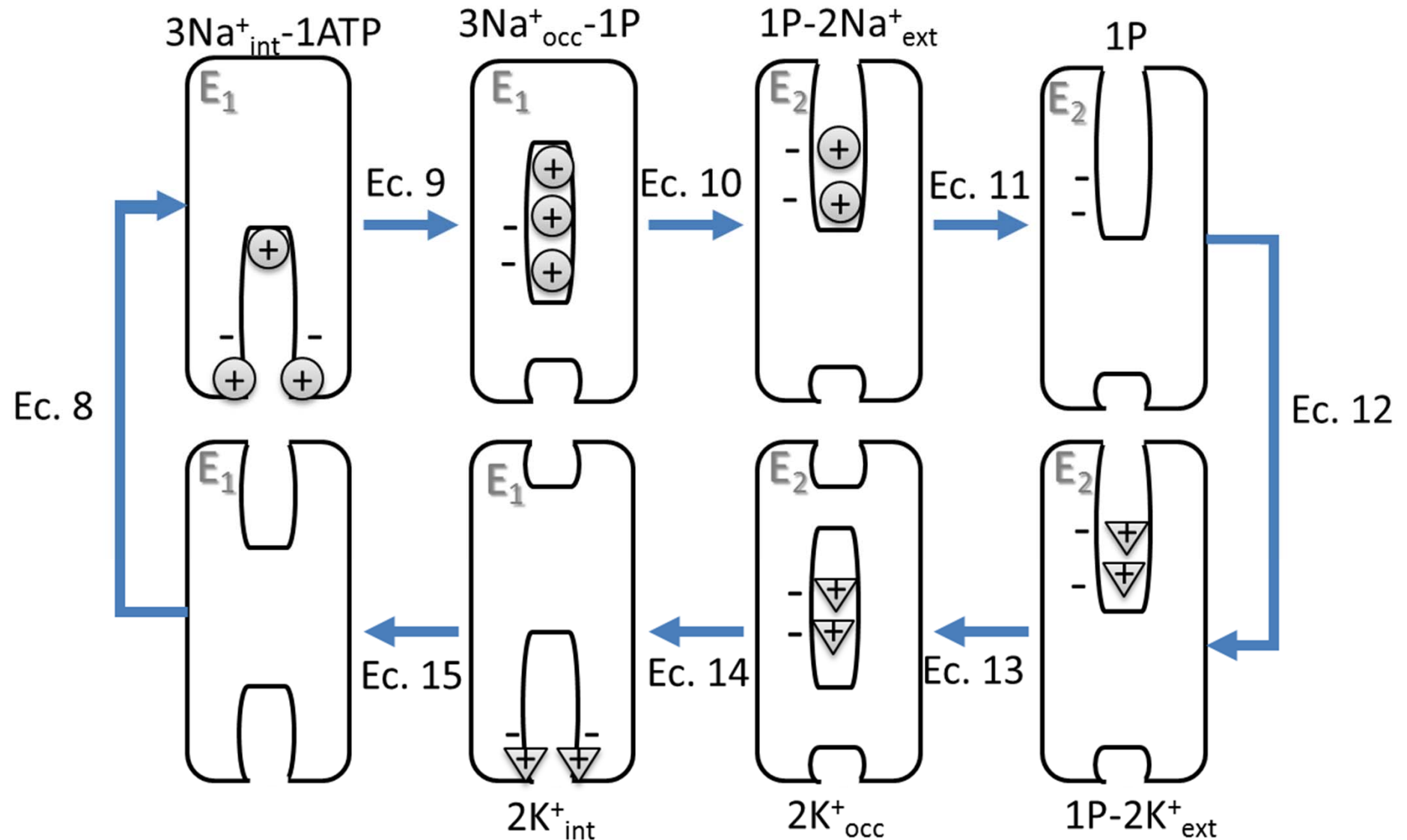
- **Sustancia química:**  $a \in V$
- **Solución o entorno químico:**  $w \in V^*$
- **Concentración de una sustancia:**  $|w|_a$ ,  $a \in V$ ,  
 $w \in V^*$
- **Reacción química:**  $R = \{\sigma_1, \sigma_2, \dots, \sigma_n\}$ ,  $n \in \mathbb{N}$ ,  
 $\sigma_i \in (Sub_V \cup Ins_V \cup Del_V)$
- **Estado del sistema** en un tiempo  $i > 0$ :  
 $C_i(x)$  para todo  $x \in X_G - \{X_I\}$

# Simulating cellular transport with PNPEP

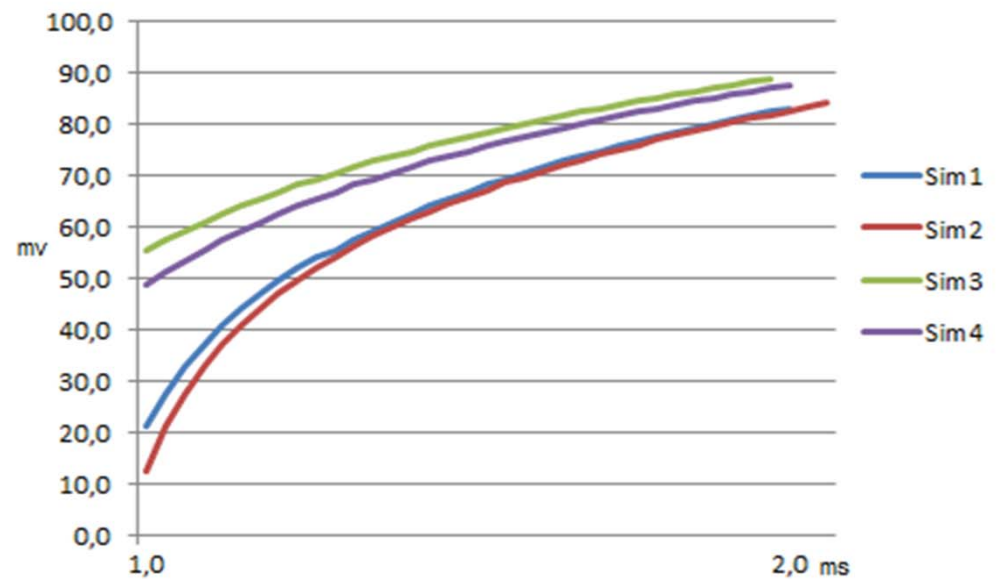
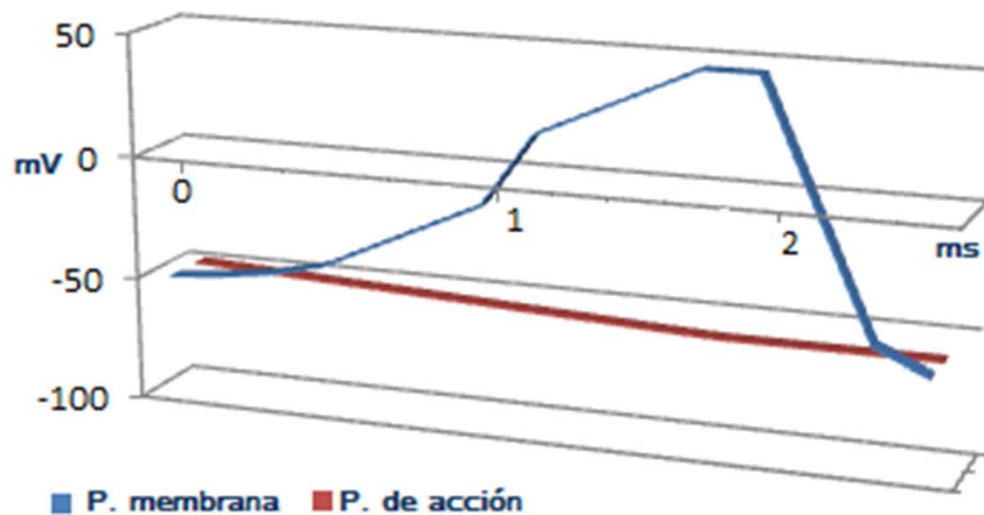
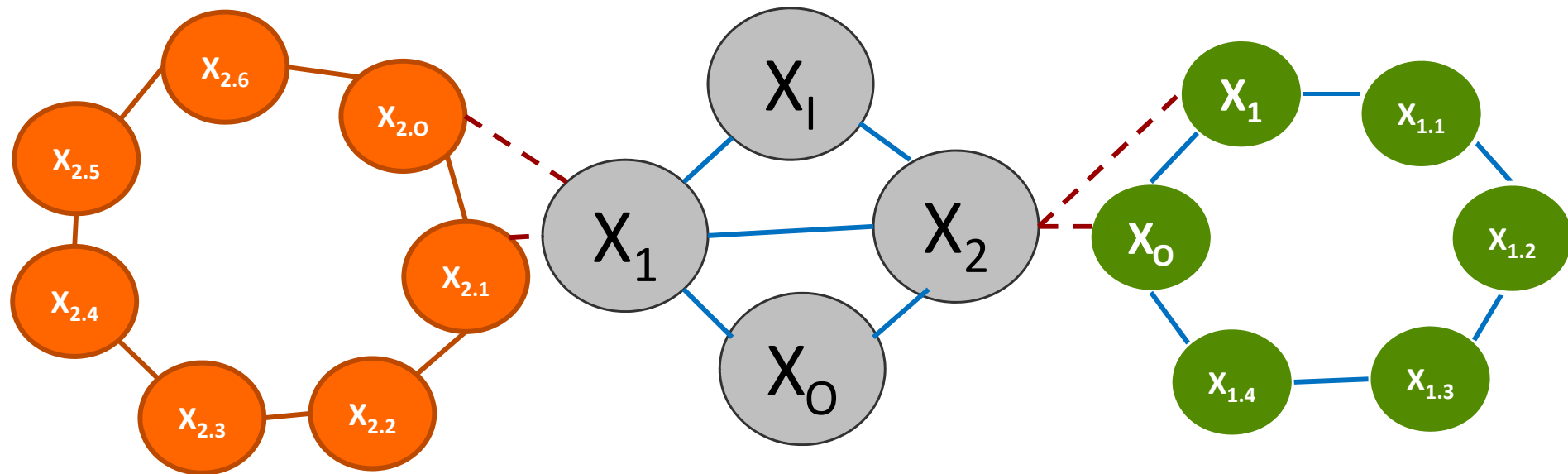
➔ Bomba Sodio-Potasio: transporte activo

	Concentración extracelular	Concentración intracelular	Potencial reposo	Potencial reposo Células excitables
Na	145 mEq/L	[5; 15] mEq/L	-20mV -120mV	-70mV
K	5mEq/L	140 mEq/L		

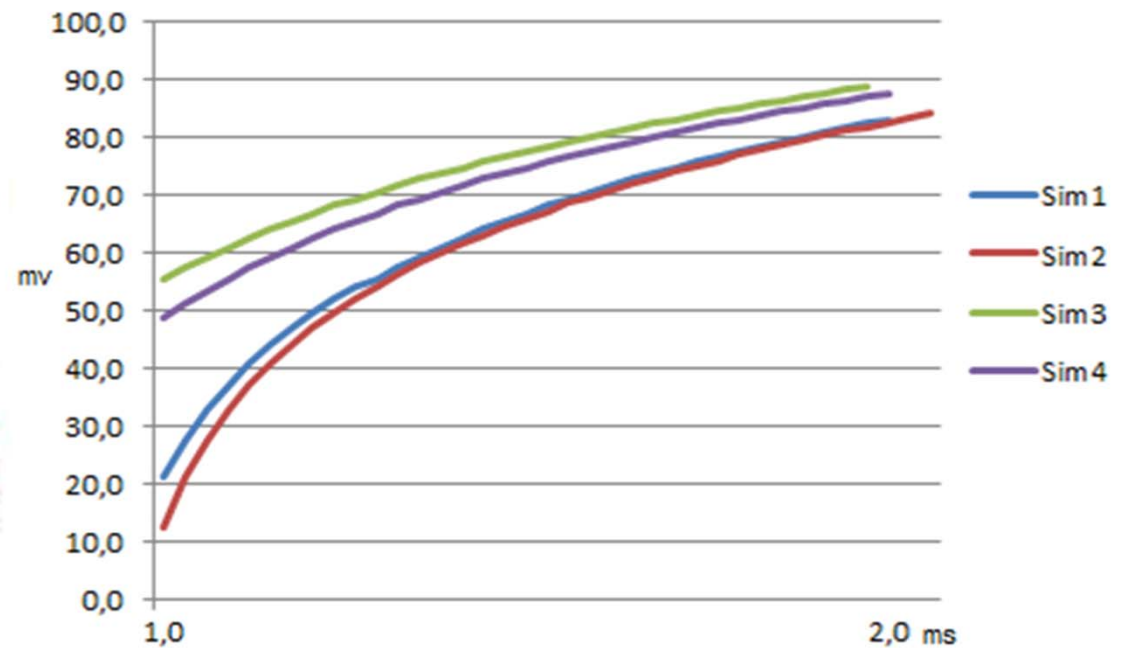
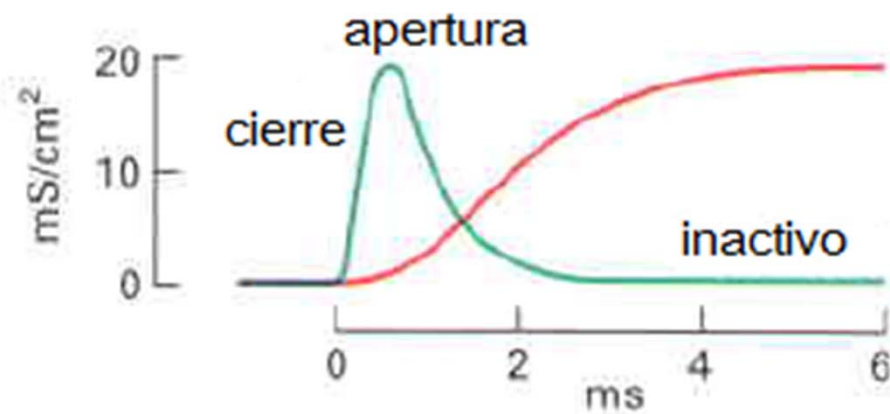
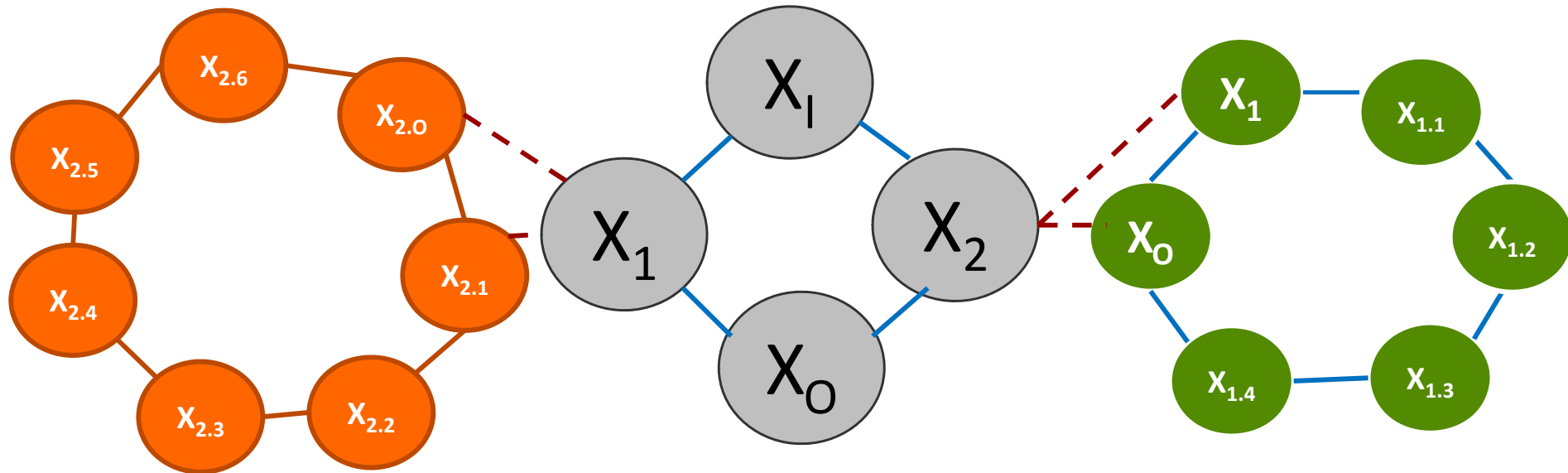
# Simulating cellular transport with PNPEP



# Simulating cellular transport with PNPEP



# NPEP Paramétricas: Bomba Na-K



# Open problems and future work

- PNPEP as a first model in a family of QNEPs - Quantitative NEPs,
  - Will may address probabilistic, estocastic, and more additional quantitative elements.
  - To study the dynamic of evoltuionary trajectory NEPs.
  - To calculate evolutionary distances
  - To classify and to distribute based on quantitative criterions
  - Behavior based on learning
  - To optimize based on multiobjctives

*Thanks for your attention*